

2917 RECEIVED Page 1 of 7

JUL 05 2001

## TECH CENTER 1600/2900

DATE: 06/12/2001  
TIME: 13:11:24

**RAW SEQUENCE LISTING**  
**PATENT APPLICATION: US/09/297,486**

DATE: 06/12/2001  
TIME: 13:11:24

Input Set : A:\GJE-30.txt  
Output Set: N:\CRF3\06122001\I297486.raw

ENTERED

4,2  
7-9-01  
P.Z.

4 <110> APPLICANT: Martin, John Francis  
 5 Yla-Herttula, Seppo  
 6 Barker, Stephen George Edward  
 8 <120> TITLE OF INVENTION: Therapeutic Use of an Agent That Stimulates NO or  
 Prostacyclin Production  
 9 and Delivery Device  
 11 <130> FILE REFERENCE: GJE-30  
 13 <140> CURRENT APPLICATION NUMBER: US 09/297,486  
**C--> 14 <141> CURRENT FILING DATE: 2001-05-24**  
 16 <150> PRIOR APPLICATION NUMBER: PCT/GB97/03015  
 17 <151> PRIOR FILING DATE: 1997-11-03  
 19 <150> PRIOR APPLICATION NUMBER: GB 9622852.3  
 20 <151> PRIOR FILING DATE: 1996-11-01  
 22 <150> PRIOR APPLICATION NUMBER: GB 9709494.0  
 23 <151> PRIOR FILING DATE: 1997-05-09  
 25 <150> PRIOR APPLICATION NUMBER: GB 9717791.9  
 26 <151> PRIOR FILING DATE: 1997-08-21  
 28 <160> NUMBER OF SEQ ID NOS: 10  
 31 <210> SEQ ID NO: 1  
 32 <211> LENGTH: 441  
 33 <212> TYPE: DNA  
 34 <213> ORGANISM: Homo sapiens  
 36 <220> FEATURE:  
 37 <221> NAME/KEY: CDS  
 38 <222> LOCATION: 1..441  
 40 <400> SEQUENCE: 1

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43 Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu	
44 1 .. 5 10 15	
46 tac ctc cac cat gcc aag tgg tcc cag gct gca ccc atg gca gaa gga	96
47 Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly	
48 20 25 30	
50 gga ggg cag aat cat cac gaa gtg gtg aag ttc atg gat gtc tat cag	144
51 Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln	
52 35 40 45	
54 cgc agc tac tgc cat cca atc gag acc ctg gtg gac atc ttc cag gag	192
55 Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu	
56 50 55 60	
58 tac cct gat gag atc gag tac atc ttc aag cca tcc tgt gtg ccg ctg	240
59 Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu	
60 65 70 75 80	
62 atg cga tgc ggg ggc tgc tgc aat gac gag ggc ctg gag tgt gtg ccc	288
63 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro	
64 85 90 95	
66 act gag gag tcc aac atc acc atg cag att atg cgg atc aaa cct cac	336
67 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His	
68 100 105 110	
70 caa qgc caq cac ata gga gag atg agc ttc cta cag cac aac aaa tgt	384

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71 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys  
72 115 120 125  
74 gaa tgc aga cca aag aaa gat aga gca aga caa gaa aaa tgt gac aag 432  
75 Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Cys Asp Lys  
76 130 135 140  
78 ccg agg cgg 441  
79 Pro Arg Arg  
80 145  
83 <210> SEQ ID NO: 2  
84 <211> LENGTH: 147  
85 <212> TYPE: PRT  
86 <213> ORGANISM: Homo sapiens  
88 <400> SEQUENCE: 2  
90 Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu  
91 1 5 10 15  
93 Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly  
94 20 25 30  
96 Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln  
97 35 40 45  
99 Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu  
100 50 55 60  
102 Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu  
103 65 70 75 80  
105 Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro  
106 85 90 95  
108 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His  
109 100 105 110  
111 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys  
112 115 120 125  
114 Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Cys Asp Lys  
115 130 135 140  
117 Pro Arg Arg  
118 145  
121 <210> SEQ ID NO: 3  
122 <211> LENGTH: 573  
123 <212> TYPE: DNA  
124 <213> ORGANISM: Homo sapiens  
126 <220> FEATURE:  
127 <221> NAME/KEY: CDS  
128 <222> LOCATION: 1..573  
130 <400> SEQUENCE: 3  
132 atg aac ttt ctg ctg tct tgg gtg cat tgg agc ctc gcc ttg ctg ctc 48  
133 Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu  
134 1 5 10 15  
136 tac ctc cac cat gcc aag tgg tcc cag gct gca ccc atg gca gaa gga 96  
137 Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly  
138 20 25 30  
140 gga ggg cag aat cat cac gaa gtg gtg aag ttc atg gat gtc tat cag  
141 Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln 144

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142	35	40	45	
144	cgc agc tac tgc cat cca atc gag acc ctg gtg gac atc ttc cag gag			192
145	Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu			
146	50	55	60	
148	tac cct gat gag atc gag tac atc ttc aag cca tcc tgt gtg ccg ctg			240
149	Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu			
150	65	70	75	80
152	atg cga tgc ggg ggc tgc tgc aat gac gag ggc ctg gag tgt gtg ccc			288
153	Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro			
154	85	90	95	
156	act gag gag tcc aac atc acc atg cag att atg cggt atc aaa cct cac			336
157	Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His			
158	100	105	110	
160	caa ggc cag cac ata gga gag atg agc ttc cta cag cac aac aaa tgt			384
161	Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys			
162	115	120	125	
164	gaa tgc aga cca aag aaa gat aga gca aga caa gaa aaa ccc tgt ggg			432
165	Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Pro Cys Gly			
166	130	135	140	
168	cct tgc tca gag cgg aga aag cat ttg ttt gta caa gat ccg cag acg			480
169	Pro Cys Ser Glu Arg Arg Lys His Leu Phe Val Gln Asp Pro Gln Thr			
170	145	150	155	160
172	tgt aaa tgt tcc tgc aaa aac aca gac tcg cgt tgc aag gcg agg cag			528
173	Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg Gln			
174	165	170	175	
176	ctt gag tta aac gaa cgt act tgc aga tgt gac aag ccg agg cgg			573
177	Leu Glu Leu Asn Glu Arg Thr Cys Arg Cys Asp Lys Pro Arg Arg			
178	180	185	190	
181	<210> SEQ ID NO: 4			
182	<211> LENGTH: 191			
183	<212> TYPE: PRT			
184	<213> ORGANISM: Homo sapiens			
186	<400> SEQUENCE: 4			
188	Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu			
189	1	5	10	15
191	Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly			
192	20	25	30	
194	Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln			
195	35	40	45	
197	Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu			
198	50	55	60	
200	Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu			
201	65	70	75	80
203	Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro			
204	85	90	95	
206	Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His			
207	100	105	110	
209	Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys			
210	115	120	125	

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212 Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Pro Cys Gly  
213 130 135 140  
215 Pro Cys Ser Glu Arg Arg Lys His Leu Phe Val Gln Asp Pro Gln Thr  
216 145 150 155 160  
218 Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg Gln  
219 165 170 175  
221 Leu Glu Leu Asn Glu Arg Thr Cys Arg Cys Asp Lys Pro Arg Arg  
222 180 185 190  
224 <210> SEQ ID NO: 5  
225 <211> LENGTH: 645  
226 <212> TYPE: DNA  
227 <213> ORGANISM: Homo sapiens  
229 <220> FEATURE:  
230 <221> NAME/KEY: CDS  
231 <222> LOCATION: 1..645  
233 <400> SEQUENCE: 5  
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236 Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu  
237 1 5 10 15  
239 tac ctc cac cat gcc aag tgg tcc cag gct gca ccc atg gca gaa gga 96  
240 Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly  
241 20 25 30  
243 gga ggg cag aat cat cac gaa gtg gtg aag ttc atg gat gtc tat cag 144  
244 Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln  
245 35 40 45  
247 cgc agc tac tgc cat cca atc gag acc ctg gtg gac atc ttc cag gag 192  
248 Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu  
249 50 55 60  
251 tac cct gat gag atc gag tac atc ttc aag cca tcc tgt gtg ccg ctg 240  
252 Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu  
253 65 70 75 80  
255 atg cga tgc ggg ggc tgc aat gac gag ggc ctg gag tgt gtg ccc 288  
256 Met Arg Cys Gly Gly Cys Asn Asp Glu Gly Leu Glu Cys Val Pro  
257 85 90 95  
259 act gag gag tcc aac atc acc atg cag att atg cgg atc aaa cct cac 336  
260 Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His  
261 100 105 110  
263 caa ggc cag cac ata gga gag atg agc ttc cta cag cac aac aaa tgt 384  
264 Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys  
265 115 120 125  
267 gaa tgc aga cca aag aaa gat aga gca aga caa gaa aaa aaa tca gtt 432  
268 Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Lys Ser Val  
269 130 135 140  
271 cga gga aag gga aag ggg caa aaa cga aag cgc aag aaa tcc cgg tat 480  
272 Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys Arg Lys Lys Ser Arg Tyr  
273 145 150 155 160  
275 aag tcc tgg agc gtg ccc tgt ggg cct tgc tca gag cgg aga aag cat 528  
276 Lys Ser Trp Ser Val Pro Cys Gly Pro Cys Ser Glu Arg Arg Lys His  
277 165 170 175

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280	ttg	ttt	gta	caa	gat	ccg	cag	acg	tgt	aaa	tgt	tcc	tgc	aaa	aac	aca	576
281	Leu	Phe	Val	Gln	Asp	Pro	Gln	Thr	Cys	Lys	Cys	Ser	Cys	Lys	Asn	Thr	
282				180				185					190				
284	gac	tcg	cgt	tgc	aag	gct	agg	cag	ctt	gag	tta	aac	gaa	cgt	act	tgc	624
285	Asp	Ser	Arg	Cys	Lys	Ala	Arg	Gln	Leu	Glu	Leu	Asn	Glu	Arg	Thr	Cys	
286				195				200				205					
288	aga	tgt	gac	aag	ccg	agg	cgg										645
289	Arg	Cys	Asp	Lys	Pro	Arg	Arg										
290				210			215										
293	<210>	SEQ	ID	NO:	6												
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295	<212>	TYPE:	PRT														
296	<213>	ORGANISM:	Homo sapiens														
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300	Met	Asn	Phe	Leu	Leu	Ser	Trp	Val	His	Trp	Ser	Leu	Ala	Leu	Leu	Leu	
301	1				5				10				15				
303	Tyr	Leu	His	His	Ala	Lys	Trp	Ser	Gln	Ala	Ala	Pro	Met	Ala	Glu	Gly	
304					20				25				30				
306	Gly	Gly	Gln	Asn	His	His	Glu	Val	Val	Lys	Phe	Met	Asp	Val	Tyr	Gln	
307					35				40				45				
309	Arg	Ser	Tyr	Cys	His	Pro	Ile	Glu	Thr	Leu	Val	Asp	Ile	Phe	Gln	Glu	
310					50				55				60				
312	Tyr	Pro	Asp	Glu	Ile	Glu	Tyr	Ile	Phe	Lys	Pro	Ser	Cys	Val	Pro	Leu	
313		65				70				75				80			
315	Met	Arg	Cys	Gly	Gly	Cys	Cys	Asn	Asp	Glu	Gly	Leu	Glu	Cys	Val	Pro	
316					85					90				95			
318	Thr	Glu	Glu	Ser	Asn	Ile	Thr	Met	Gln	Ile	Met	Arg	Ile	Lys	Pro	His	
319					100				105				110				
321	Gln	Gly	Gln	His	Ile	Gly	Glu	Met	Ser	Phe	Leu	Gln	His	Asn	Lys	Cys	
322					115				120				125				
324	Glu	Cys	Arg	Pro	Lys	Lys	Asp	Arg	Ala	Arg	Gln	Glu	Lys	Lys	Ser	Val	
325					130				135				140				
327	Arg	Gly	Lys	Gly	Gly	Gln	Lys	Arg	Lys	Arg	Lys	Lys	Ser	Arg	Tyr		
328		145				150				155				160			
330	Lys	Ser	Trp	Ser	Val	Pro	Cys	Gly	Pro	Cys	Ser	Glu	Arg	Arg	Lys	His	
331					165				170				175				
333	Leu	Phe	Val	Gln	Asp	Pro	Gln	Thr	Cys	Lys	Cys	Ser	Cys	Lys	Asn	Thr	
334					180				185				190				
336	Asp	Ser	Arg	Cys	Lys	Ala	Arg	Gln	Leu	Glu	Leu	Asn	Glu	Arg	Thr	Cys	
337					195				200				205				
339	Arg	Cys	Asp	Lys	Pro	Arg	Arg										
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348	<220>	FEATURE:															
349	<221>	NAME/KEY:	CDS														
350	<222>	LOCATION:	1..696														

**VERIFICATION SUMMARY**

PATENT APPLICATION: US/09/297,486

DATE: 06/12/2001

TIME: 13:11:25

Input Set : A:\GJE-30.txt

Output Set: N:\CRF3\06122001\I297486.raw

L:14 M:271 C: Current Filing Date differs, Replaced Current Filing Date